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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,727	01/17/2002	Graham D. Cook	1142.0125-00	2584

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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/046,727	COOK ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-13 and 26-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-13 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed June 20, 2006 have been received and entered into the application.

Action Summary

The rejection of claims 2 and 6-13 under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) of record in view of White (U.S.Patent No. 5,431,916) is being maintained for the reasons stated in the previous Office Action and the rejection is modified in this Office Action to exclude cancelled claims and to include newly added claim 26.

The rejection of claims 1, 2 and 7-13 under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) of record in view of Weng et al. (U.S.Patent No. 5,512,300) and further in view of Ouali et al. (U.S.Patent No. 6287600) is being maintained for the reasons stated in the previous Office Action and the rejection is modified in this Office Action to exclude cancelled claims.

Applicant's amendment necessitated additional rejection presented in this Office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-13 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) of record in view of White (U.S.Patent No. 5,431,916).

Sunshine et al. teach a pharmaceutical composition comprising 50-400mg ibuprofen and from about 12.5-50mg diphenhydramine elicits an enhanced analgesic and/or anti-inflammatory response. (abstract, column 6, lines 44-45, column 7, lines 1-4, column 14, claim 39). Sunshine et al. also teach that polyethylene glycol is an acceptable carrier to the above composition (column 7, lines 31-35). Sunshine et al. teach the above composition can be formulated in capsules. (column 7, lines 20-23, claim 41). Sunshine et al. teach that diphenhydramine is commercially available as the hydrochloride salt. (column 1, lines 60-65). Sunshine et al. teach the above composition can be formulated in tablet form or two or more layered tablets. (column 8, lines 4-10). Sunshine et al. teach that diphenhydramine is commercially available as the hydrochloride salt. (column 1, lines 60-65).

Sunshine et al. do not teach the composition formulated in a **soft gelatin** capsule.

White teaches a composition comprising ibuprofen, diphenhydramine and polyethylene glycol can be formulated in soft gelatin capsule. (column 5, lines 20-65, column 6, lines 65-68, column 7, lines 5-25, Example 11, claims 13 and 15). White discloses that soft gelatin capsules are convenient, portable and easy to swallow and

offer a simple means of masking the unpleasant taste and aromas of many pharmaceutically acceptable actives. (column 1, lines 25-31).

It would have been obvious to one of ordinary skill in the art to formulate Sunshine composition into soft gelatin capsules because the composition can be formulated in capsule form in general as taught by Sunshine et al. and it is well-known by White that the composition comprising diphenhydramine and ibuprofen can be formulated in soft gelatin capsules. One would have been motivated to formulate Sunshine composition to soft gelatin capsules in to achieve provide convenient, portable and easy to swallow capsule as taught by White. Further, that soft gelatin capsules are advantageously offer a simple means of masking the unpleasant taste and aromas of many pharmaceutically acceptable actives. One would have been motivated to deliver the composition taught by Sunshine in a soft gelatin capsules that are portable and easy to swallow and to avoid the unpleasant taste of the actives. (ibuprofen and diphenhydramine). Moreover, Applicants' recitation in claim 26 and the intended use of polyethylene glycol in claim 6 do not represent a patentable limitation in a composition claims since it fails to impart any physical limitation to the composition.

Claims 1 and 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) of record in view of Weng et al. (U.S.Patent No. 5,512,300) and further in view of Ouali et al. (U.S.Patent No. 6287600).

Sunshine et al. teach a pharmaceutical composition comprising 50-400mg ibuprofen and from about 12.5-50mg diphenhydramine elicits an enhanced analgesic

and/or anti-inflammatory response. (abstract, column 6, lines 44-45, column 7, lines 1-4, column 14, claim 39). Sunshine et al. also teach that polyethylene glycol is an acceptable carrier to the above composition (column 7, lines 31-35). Sunshine et al. teach the above composition can be formulated in tablet form or two or more layered tablets. (column 8, lines 4-10). Sunshine et al. teach that diphenhydramine is commercially available as the hydrochloride salt. (column 1, lines 60-65).

Sunshine et al. do not teach the separation of ibuprofen and diphenhydramine in bilayer tablet formulation.

Weng et al. report that it has been recognized that solid dosage forms such as tablets containing ibuprofen and other ingredients tend to exhibit stability problems, including the formulation of low melting point eutectics. (column 1, lines 13-20). Weng et al. report ibuprofen forms low melting point eutectics with diphenhydramine hydrochloride. (column 1, lines 55-57).

Ouali et al. teach that bilayer tablets have advantages in that it is easier and more economical to manufacture than prior compositions that separate a first drug and a second drug into physically discrete regions of a single dosage form. (column 7, lines 30-41).

It would have been obvious to one of ordinary skill in the art to separate diphenhydramine and ibuprofen of Sunshine composition in a bilayer tablet because diphenhydramine and ibuprofen in a solid dosage forms such as tablets tend to exhibit stability problems including the formation of eutectics as taught by Weng et al. and because bilayer formulation of Sunshine composition has advantage of separate a first

drug and a second drug into physically discrete regions of a single dosage form as taught by Ouali et al. One would have been motivated to separate ibuprofen and diphenhydramine bilayer tablet into physically discrete region of a single bilayer tablets in order to avoid the eutectic stability problems of solid dosage form comprising diphenhydramine and ibuprofen reported by Wang et al.

Claims 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sunshine et al. (U.S.Patent No. 4,522,826) of record in view of Weng et al. (U.S.Patent No. 5,512,300) and further in view of Ouali et al. (U.S.Patent No. 6287600) and Drug Facts and Comparisons, 1997 Edition.

Sunshine et al. teach a pharmaceutical composition comprising 50-400mg ibuprofen and from about 12.5-50mg diphenhydramine elicits an enhanced analgesic and/or anti-inflammatory response. (abstract, column 6, lines 44-45, column 7, lines 1-4, column 14, claim 39). **Sunshine et al. teach that "propionic acid derivatives" including ibuprofen is defined as non-narcotic analgesics/nonsteroidal anti-inflammatory drugs having free –CH(CH3)COOH. (column 5, lines 1-20, particularly, lines 12-15).** Sunshine et al. also teach that polyethylene glycol is an acceptable carrier to the above composition (column 7, lines 31-35). Sunshine et al. teach the above composition can be formulated in tablet form or two or more layered tablets. (column 8, lines 4-10). Sunshine et al. teach that diphenhydramine is commercially available as the hydrochloride salt. (column 1, lines 60-65). **Sunshine et al. teach that the composition can be formulated with for oral administration in the form of tablets or capsules with any oral non-toxic pharmaceutically**

acceptable inert carrier such as lactose, starch cellulose and carboxymethylcellulose. (column 7, lines 15-45).

Sunshine et al. do not teach the separation of ibuprofen and diphenhydramine in Sunshine's bilayer tablet formulation and the onset of action within 60 minutes.

Weng et al. report that it has been recognized that solid dosage forms such as tablets containing ibuprofen and other ingredients tend to exhibit stability problems, including the formulation of low melting point eutectics. (column 1, lines 13-20). Weng et al. report ibuprofen forms low melting point eutectics with diphenhydramine hydrochloride. (column 1, lines 55-57).

Ouali et al. teach that bilayer tablets have advantages in that it is easier and more economical to manufacture than prior compositions that separate a first drug and a second drug into physically discrete regions of a single dosage form. (column 7, lines 30-41).

Drug Facts and Comparisons teach that onset of action of antihistamines including diphenhydramine is within 15 to 30 minutes (page 1135, under Antihistamines: Dosage and Effects; page 1136 under Pharmacokinetics). Drug Facts and Comparisions teach that onset of action of ibuprofen is 0.5 hour (30 minutes). (Page 1387, under pharmacokinetic parameters).

It would have been obvious to one of ordinary skill in the art to separate diphenhydramine and ibuprofen of Sunshine composition in a bilayer tablet because diphenhydramine and ibuprofen in a solid dosage forms such as tablets tend to exhibit stability problems including the formation of eutectics as taught by Weng et al. and

because bilayer formulation of Sunshine composition has advantage of separate a first drug and a second drug into physically discrete regions of a single dosage form as taught by Ouali et al. One would have been motivated to separate ibuprofen and diphenhydramine bilayer tablet into physically discrete region of a single bilayer tablets in order to avoid the eutectic stability problems of solid dosage form comprising diphenhydramine and ibuprofen reported by Wang et al.

With regard to limitation of onset of action within 60 minutes, it would have been obvious to one of ordinary skill in the art that the composition comprising ibuprofen and diphenhydramine as modified by Weng et al. and Ouali et al. would have an effect within 60 minutes as claimed by the Applicants because Drug Facts and Comparison teaches that each of the active agents have onset of action within 30 minutes. For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Response to Arguments

Applicants' arguments filed June 20, 2006 have been fully considered but they are not persuasive. With regard to arguments regarding Sunshine in view of White, Applicants argue there is no teaching or suggestion in any of the cited references to modify their teachings to arrive at the claimed invention because Sunshine fails to

specifically disclose the claimed composition including polyethylene glycol in combination with ibuprofen and diphenhydramine and it is improper for the Office to pick and choose polyethylene glycol from the list of binders in hindsight, as a mere list of compounds in Sunshine does not direct one of ordinary skill in the art to use polyethylene glycol. This is not persuasive because it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In this case, Sunshine teaches polyethylene glycol is a suitable binder to be employed in the composition comprising ibuprofen and diphenhydramine and additionally White also teaches that polyethylene glycol is suitable in the composition comprising ibuprofen and diphenhydramine because polyethylene glycol facilitates the solubility of actives. (column 7, lines 20-30). White further teaches the process of making the encapsulated pharmaceutical composition comprising diphenhydramine and ibuprofen by adding polyethylene glycol. (column 14, claim 15). Therefore one of ordinary skill in the art would have been motivated to employ well-known suitable binder, polyethylene glycol, well-kwon to be employed in the composition comprising ibuprofen and diphenhydramine by Sunshine and White and suitable for employing for the process of making such composition taught by White to facilitate the solubility of the actives and to successfully formulate a soft gelatin capsules combining the two actives.

With regard to arguments regarding claims 1 and 7-13 unpatentable over Sunshine in view of Weng and further in view of Quali, Applicants essentially argue that there is no motivation to arrive at the claimed composition which contains all three of ibuprofen, diphenhydramine and polyethylene glycol in a bilayer tablet as they teach coating or chemical modification of an NSAID, including Weng fails to contemplate the advantages of ibuprofen free acid over salt forms, Quali teaches that the interaction between an NSAID and prostaglandin is prevented by the enteric coating. This is not persuasive because the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it is well known by Sunshine et al. that ibuprofen free acid and diphenhydramine can be combined in a single bilayer tablet formulation with usual excipients set forth in instant claim 30, eliciting an enhanced analgesic properties; it is well known that these two active agents combined have a stability problems by Weng et al.; that advantages of bilayer tablet formulation are well known by Quali et al. Therefore, it would have been *prima facie* obvious to formulate a composition comprising ibuprofen and diphenhydramine in a single bilayer formulation in two different layers in order to achieve a stable formulation eliciting enhanced analgesic properties. It is the Examiner's position that while the combination comprising ibuprofen free acid and

diphenhydramine in a bilayer tablet is well known by Sunshine having synergistic effect is well known, it is also known that there is stability problem when ibuprofen and diphenhydramine are physically mixed together in a single layer as taught by Weng et al. Weng et al. clearly report that there is a stability problem in a mixture of diphenhydramine hydrochloride and ibuprofen resulting eutectic mixture. Therefore One would have been motivated to separate bilayer tablet taught by Sunshine containing ibuprofen and diphenhydramine mixed in a single layer to two different layer in order to avoid the problem of the two active agents forming an eutectic mixture in a single layer within the bilayer tablet. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sreenivasan Padmanabhan
Supervisory Primary Examiner
Art Unit 1617

Jmk

August 25, 2006